

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-13 – Canceled.

14. (Previously Presented) A method for constitutive and/or inducible gene knock down in a vertebrate, or in a tissue culture or cells of a cell culture derived from a vertebrate, which method comprises stably integrating an expression vector comprising a short hairpin RNA construct under control of a ubiquitous promoter into the genome of the vertebrate, of the tissue culture or of the cells of the cell culture.

15. (Currently Amended) The method of claim [[1]] 14, wherein the expression vector is suitable for stable integration into the genome of a vertebrate, or into the genome of the tissue culture or of cells of the cell culture.

16. (Currently Amended) The method of claim [[1]] 14, wherein the expression vector contains homologous sequences suitable for integration at a defined genomic locus through homologous recombination in the genome of the vertebrate, in the genome of the tissue culture or in the genome of the cells of the cell culture.

17. (Currently Amended) The method of claim [[3]] 16, wherein the cells of the cell culture are embryonic cells.

18. (Currently Amended) The method of claim [[3]] 16, wherein the homologous sequences are suitable for integration at a polymerase II dependent locus in the genome of the vertebrate, in the genome of the tissue culture or in the genome of the cells of the cell culture.

19. (Currently Amended) The method of claim [[1]] 14, wherein the expression vector

further contains functional sequences selected from the group consisting of splice acceptor sequences, polyadenylation sites and selectable marker sequences.

20. (Currently Amended) The method of claim [[5]] 18, wherein the polymerase II dependent locus is selected from the group consisting of a Rosa26, collagen, RNA polymerase, actin and HPRT locus.

21. (Currently Amended) The method of claim [[1]] 14, wherein the ubiquitous promoter is selected from the group of promoters consisting of polymerase I, II and III dependent promoters.

22. (Currently Amended) The method of claim [[8]] 21, wherein the ubiquitous promoter is selected from the group consisting of a polymerase II or III dependent promoter.

23. (Currently Amended) The method of claim [[8]] 21, wherein the ubiquitous promoter is selected from the group consisting of a CMV promoter, a CAGGS promoter, a snRNA promoter, a RNase P RNA promoter, a tRNA promoter, a 7SL RNA promoter and a 5 S rRNA promoter.

24. (Currently Amended) The method of claim [[10]] 23, wherein the S nRNA promoter is a U6 promoter.

25. (Currently Amended) The method of claim [[10]] 23, wherein the RNase P RNA promoter is a H1 promoter.

26. (Currently Amended) The method of claim [[1]] 14, wherein the ubiquitous promoter is a constitutive promoter.

27. (Currently Amended) The method of claim [[1]] 14, wherein the ubiquitous promoter is an inducible promoter.

28. (Currently Amended) The method of claim [[14]] 27, wherein the inducible promoter

contains an operator sequence selected from the group consisting of tet, Gal4 and lac.

29. (Currently Amended) The method of claim [[1]] 14, wherein said vertebrate is a non-human vertebrate.

30. (Currently Amended) The method of claim [[16]] 29, wherein the non-human vertebrate is selected from the group of vertebrates consisting of mouse and fish.

31. (Currently Amended) The method of claim [[1]] 14, wherein the expression vector is a Pol III dependent promoter driven shRNA construct suitable to be integrated into a ubiquitously active Pol II dependent locus;

32. (Currently Amended) The method of claim [[18]] 31, wherein the PolIII dependent promoter is selected from a constitutive H1 promoter and a constitutive U6 promoter.

33. (Currently Amended) The method of claim [[1]] 14, wherein the expression vector is a Pol III dependent promoter driven shRNA construct suitable to be integrated into a ubiquitously active Pol II dependent locus.

34. (Currently Amended) The method of claim [[20]] 33, wherein the Pol III dependent promoter is selected from an inducible U6 promoter and an inducible H1 promoter.

35. (Currently Amended) The method of claim [[1]] 14, wherein the expression vector is a Pol II dependent promoter driven shRNA construct suitable to be integrated into a ubiquitously active Pol II dependent locus.

36. (Currently Amended) The method of claim [[22]] 35, wherein the Pol III dependent promoter is a inducible CMV promoter.

37. (Currently Amended) The method of claim [[1]] 14, wherein the shRNA comprises

(I) at least one DNA segment A-B-C wherein

A is a 15 to 35, ~~preferably 19 to 29~~ bp DNA sequence with at least 95%, ~~preferably 100%~~ complementarity to the gene to be knocked down;

B is a spacer DNA sequence having 5 to 9 bp forming the loop of the expressed RNA hair pin molecule, and

C is a 15 to 35, ~~preferably 19 to 29~~ bp DNA sequence with at least 85% complementarity to the sequence A, and

(II) a stop and or polyadenylation.

38. (Currently Amended) The method of claim ~~[[24]]~~ 37, wherein A is a 19 to 29 bp sequence with 100% complementarity to the gene to be knocked down.

39. (Currently Amended) The method of claim ~~[[1]]~~ 14, wherein the expression vector is integrated at a polymerase dependent locus of the living organism, tissue culture or cell culture.

40. (Currently Amended) The method of claim ~~[[1]]~~ 14, wherein the method for constitutive and/or inducible gene knock down in a vertebrate comprises integrating the expression vector into ES cells of the vertebrate.

41. (Currently Amended) A vertebrate, or tissue or cell culture derived from a vertebrate having stably integrated, preferably at a polymerase II dependent locus of the vertebrate, tissue culture or cells of the cell culture, an expression vector comprising a short hairpin RNA construct under control of a ubiquitous promoter.

42. (Currently Amended) The vertebrate tissue or cell culture of claim ~~[[28]]~~ 41, which is or is derived from a non-human vertebrate.

43. (Currently Amended) The vertebrate of claim ~~[[29]]~~ 42, which is selected from the group of vertebrates consisting of mouse and fish.

44. (Previously Presented) An expression vector comprising a short hairpin RNA construct under control of a ubiquitous promoter.